

Short communication

Using doubly-labeled water measurements of human energy expenditure to estimate inhalation rates

Marc Stifelman*

*U.S. Environmental Protection Agency, Region 10, Office of Environmental Assessment, Risk Evaluation Unit, 1200 Sixth Avenue,
Mail Stop: OEA-095, Seattle, Washington 98101, United States*

Received 25 August 2006; received in revised form 24 November 2006; accepted 28 November 2006
Available online 17 January 2007

Abstract

Doubly-labeled water (DLW) data is recognized as an improvement over alternative methods to quantify human energy expenditure. Previously, energy expenditure has been estimated indirectly using heart-rate monitoring, calorimetry, or accelerometer measurements. Inhalation rate estimates can benefit from improved energy expenditure estimates using equations developed by Layton. DLW methods are advantageous for several reasons: the database is robust, they are direct measures, subjects are free-living, and the observation period is longer than what is possible from staged activity measures. DLW energy data is an improvement over previous inhalation estimates based on dietary recall survey data. Mean long-term inhalation rates of 16 m³/day and 13 m³/day, for physically active adult men and women, respectively, were derived based on DLW estimates of energy expended. The range of human energy expenditure is narrow with the maximum energy expenditure not likely greater than twice the minimum.

Published by Elsevier B.V.

Keywords: Inhalation; Risk assessment; Energy expenditure; Doubly-labeled water

1. Introduction

Previously, Stifelman described a method to estimate inhalation rates based on Layton's metabolic approach (Layton, 1993; Stifelman, 2003). Since that time, a significant body of data using doubly-labeled water (DLW) methods has been compiled to measure energy expenditure in free-living people (Food and Agriculture Organization of the United Nations (FAO), 2004a; Institute of Medicine (IOM) Panel on Macronutrients, 2005). The DLW data is recognized as a significant improvement over previous methods used to quantify

human energy expenditure (Black et al., 1996; Schoeller, 1999; Shetty, 2002). The Layton inhalation estimates were based on food intakes from NHANES dietary recall survey data (Layton, 1993). As such, the intake estimates are subject to recall bias and are not necessarily equal to expenditure, but the relationship between energy expenditure and inhalation rates remains valid (Westerterp et al., 1986; Garrow, 1988; Black et al., 1993; Layton, 1993; Shetty, 2002). Utilization of the improved DLW energy expenditure data in conjunction with Layton's equations to convert metabolic energy to daily inhalation rates will reduce uncertainties in inhalation rate estimates and provide internal consistency between air and food exposure pathways.

* Tel.: +1 206 553 6979; fax: +1 206 553 0119.
E-mail address: stifelman.marc@epa.gov.

DLW measurements are more representative of human behavior because they utilize free-living subjects monitored over a duration of weeks (Black et al., 1996). DLW measurements avoid errors associated with indirect methods, using heart rate measures during staged activities to estimate energy expenditure or inhalation rates (Shetty, 2002). The longer observation period reduces uncertainties associated with using activity studies of short duration to infer inhalation rates over longer periods of time (Stifelman, 2003). Staged activity studies may remain useful as measures of acute exposure associated with specific activities performed during a defined period of time, but their utility to quantify long-term exposures associated with chronic health effects is limited.

2. Doubly-labeled water energy expenditure methodology

Although DLW was initially developed to measure energy expenditure in small mammals, it has been widely applied to human subjects (Shetty, 2002). The current recommended levels of caloric intakes and activity levels prepared by the U.S. Institute of Medicine and the World Health Organization are based on DLW data (FAO, 2004a; IOM, 2005). Briefly, the DLW method administers two forms of stable isotopically labeled water: 1) deuterium-labeled ($^2\text{H}_2\text{O}$) and 2) $^{18}\text{oxygen}$ -labeled (H_2^{18}O). The disappearance of the hydrogen-labeled $^2\text{H}_2\text{O}$ represents the total water flux while the disappearance of the oxygen-labeled H_2^{18}O represents the sum of water flux and CO_2 generated from respiration. The difference in disappearance rates between the two isotopes represents the energy expended over a period of 1–3 half-lives of the labeled water. The resulting duration of observation is typically 1–3 weeks, depending on the size and activity level of the subject.

3. Doubly-labeled water energy expenditure database

The DLW energy expenditure database includes subjects from around the world representing a diversity of ethnicity, age, activity, body type, and fitness level (FAO, 2004a; IOM, 2005). Approximately 3000 DLW measurements used by the Institute of Medicine are available on the IOM Website the following address: <http://www.iom.edu/file.asp?id=7302>. The IOM report is available at: <http://books.nap.edu/catalog/10490.html>. The United Nations, FAO report is available at: <ftp://ftp.fao.org/docrep/fao/007/y5686e/y5686e00.pdf>.

4. Equating energy expenditure with inhalation rate

The following equation was used to convert daily measures energy expenditure into inhalation rates from (Layton, 1993):

$$V_E = E \times H \times VQ$$

V_E minute ventilation volume liters per minute
(1 L/min = 1.44 m³/day)

H volume of O_2 in liters consumed per kJ expended (0.05 L O_2 /kJ)

E energy expenditure kJ per day
(1 kJ = 0.239 kcal)

VQ ventilatory equivalent ratio of V_E to V_{O_2}
unitless (both quantities are liters per minute),
 $VQ = 27$ (unitless ratio).

5. Range of long-term physical activity levels

Physical activity is categorized by into four levels of activity, described in Table 1. The IOM Physical Activity Level (PAL) categories are associated with specific ranges of (elective) activity levels. A PAL is the ratio of total energy expended divided by basal metabolic rate (BMR), defined as the minimum level of energy needed to support essential physiologic functions in free-living people. Because PALs are scaled measures of physical activity, they apply to a wide range of body sizes and types. Total energy expenditure, in units of kilocalories (kcal) or megajoule (MJ), can be estimated from a PAL by multiplying by the BMR. The BMR is well-defined by standard equations based on age, gender, and body mass (Schofield, 1985; FAO, 2004a).

Table 1
IOM physical activity categories illustrated by equivalent walking distance — adapted from Brooks et al. (2004)

PAL category	PAL midpoint value (range)	Equivalent walking distance (km per day) in addition to energy expended during normal daily life (based on a 70 kg adult walking 5–6 km per hour)
Sedentary	1.25 (1.0–1.39)	0
Low active	1.5 (1.4–1.59)	3.5
Active	1.75 (1.6–1.89)	11.7
Very active	2.2 (1.9–2.5)	26.9

As seen from Table 1, the very active (i.e., PAL range 1.9–2.5) designation is equivalent to a walking distance of approximately 27 km per day. It is unlikely that this level of daily activity would be exceeded over a duration of years. Both IOM and FAO recommend achieving a PAL of 1.7 to maintain a healthy body mass and to reduce the risk of various chronic diseases. The relationship between PAL, equivalent walking distance, and inhalation rate is depicted in Fig. 1.

For comparison, a PAL of 1.6 has been described as a mode for adults in affluent societies (Black et al., 1996). PALs exceeding the IOM and FAO ranges are generally not sustainable over long periods of time, but can be quite high for limited periods of time (Westerterp, 2001). As an extreme example, DLW measurements of Tour de France cyclists had PALs ranging from 4.3 to 5.3 during the course of the race (Westerterp et al., 1986). The IOM and FAO PAL describe a range of 1.4–2.5 in accord with ranges of sustainable PALs described by others, including people actively engaged in non-mechanized agriculture, deployed military personnel, and long-distance runners (Haggarty et al., 1994; Black et al., 1996; Westerterp, 1998; Westerterp, 2001). DLW studies of elite athletes and deployed military personnel demonstrated that people will experience a negative energy balance, that is weight loss, for PALs exceeding 2–2.5 (Westerterp, 1998). Neither a negative nor

positive energy balance is sustainable or healthy over the long-term (IOM, 2005).

6. Using DLW energy measurements to estimate inhalation rates

Both the IOM and FAO reports recommend energy expenditure levels organized by body size, gender, and age. The recommendations provide a healthy level of activity sufficient to reduce risk of chronic disease and to maintain body weight within a healthy body mass index range of 18.5–24.9 kg/m² (IOM, 2005). The recommended PAL levels for active and very active logically correspond to central tendency exposure (CTE) and reasonable maximum exposure (RME) contact rates used in risk assessments. The U.S. Environmental Protection Agency defines RME as a high level of exposure to ensure an adequate, but reasonable level of protection (U.S. Environmental Protection Agency Office of Solid Waste And Emergency Response, 1989). The RME distinguishes between scenarios that are possible, but highly improbable, and those that are more likely to occur within a population, with the latter being favored in risk assessment. The recommended activity levels have been identified as healthy levels, although average activity levels in affluent societies are less than the

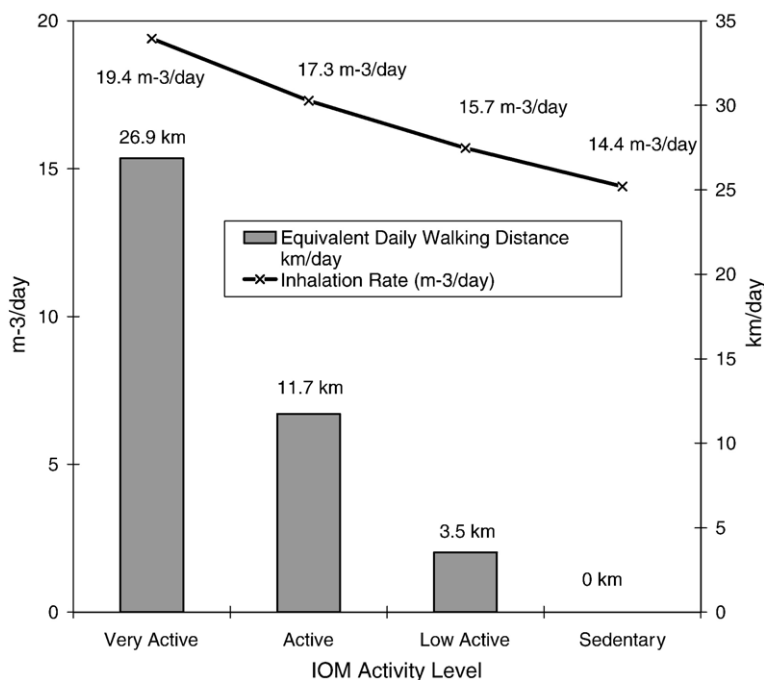


Fig. 1. IOM physical activity categories illustrated by equivalent walking distance and corresponding inhalation rate — adapted from Brooks et al. (2004).

Table 2
Summary of Institute of Medicine energy expenditure recommendations for active and very active people with equivalent inhalation rates

Age	Male energy expenditure	Inhalation rate	Female energy expenditure	Inhalation rate
Years	Active–very active (kcal/day)	Active–very active (m ³ /day)	Active–very active (kcal/day)	Active–very active (m ³ /day)
<1	607	3.4	607	3.4
1	869	4.9	869	4.9
2	1050	5.9	977	5.5
3	1485–1683	8.4–9.5	1395–1649	7.9–9.3
4	1566–1783	8.8–10.1	1475–1750	8.3–9.9
5	1658–1894	9.4–10.7	1557–1854	8.8–10.5
6	1742–1997	9.8–11.3	1642–1961	9.3–11.1
7	1840–2115	10.4–11.9	1719–2058	9.7–11.6
8	1931–2225	10.9–12.6	1810–2173	10.2–12.3
9	2043–2359	11.5–13.3	1890–2273	10.7–12.8
10	2149–2486	12.1–14.0	1972–2376	11.1–13.4
11	2279–2640	12.9–14.9	2071–2500	11.7–14.1
12	2428–2817	13.7–15.9	2183–2640	12.3–14.9
13	2618–3038	14.8–17.2	2281–2762	12.9–15.6
14	2829–3283	16.0–18.5	2334–2831	13.2–16.0
15	3013–3499	17.0–19.8	2362–2870	13.3–16.2
16	3152–3663	17.8–20.7	2368–2883	13.4–16.3
17	3226–3754	18.2–21.2	2353–2871	13.3–16.2
18	3263–3804	18.6–21.5	2336–2858	13.2–16.1
19–30	3015–3490	17.0–19.7	2373–2683	13.4–15.2
31–50	2862–3338	16.2–18.9	2263–2573	12.8–14.5
51–70	2671–3147	15.1–17.8	2124–2435	12.0–13.8

recommended levels (IOM, 2005). To be consistent with the recommendations for a more active lifestyle, only the higher levels of activity are considered.

The IOM and FAO recommendations are very similar to one another. For the sake of brevity and relevance to risk assessment only the IOM levels for active and very active males and females of average body mass are summarized by age in Table 2. The energy levels are based on IOM and the corresponding inhalations rates were calculated by this author using Layton's equations. For any given risk assessment, parameters could be selected differently to reflect the age, body mass, gender, intensity, and duration of exposure of the target population. Table 3 compares the recommended CTE and RME inhalation rates for males and females ages 1–5 and 19–70 current guidance issued by the U.S. Environmental Protection Agency.

7. Application to aboriginal populations

It has been suggested that inhalation rates associated with aboriginal subsistence populations may be as high as 30 m³/day (Harper et al., 2002). Harper has argued that Native Americans may not be adequately protected

by inhalation rates representative of modern or urban lifestyles, but the available literature does not support this conclusion (Esparza et al., 2000; Harper et al., 2002; Harper et al., 2003; FAO, 2004a). A study which compared energy expenditure between “urbanized” Pima Indians residing in the U.S. and Pima Indians living a traditional lifestyle in a remote mountainous region of Mexico (Esparza et al., 2000). A traditional lifestyle demanded significantly greater energy expenditures (3289±454 kcal per day and PAL of 1.97±0.34) than a comparatively urban lifestyle (2671±454 kcal per day and a PAL of 1.57±0.16) (Esparza et al., 2000). The traditional Pima lifestyle falls within the IOM very active category while the urban Pima lifestyle is bounded by the low active category (Esparza et al., 2000; IOM, 2005).

At the population level, traditional subsistence lifestyles are likely to require more energy than urban or suburban lifestyles (Esparza et al., 2000; Harper et al., 2002; FAO, 2004a). A subsistence or rural population will require more energy than an urban or suburban population to the extent that it includes a larger proportion of active individuals (FAO, 2004b). Energy needs are largely determined by the intensity and duration of daily activities, regardless if they are spent at work, gathering food, or in leisure or athletic activities (remaining determinants of energy include age, gender, and body weight) (Schofield, 1985; Westerterp, 2001). Studies have documented extremely high energy expenditures by men employed in sedentary

Table 3
Comparison of recommended DLW-derived inhalation rates with current recommendations from U.S. environmental protection agency

Inhalation rate source	Citation	Exposure level	Inhalation rate (m ³ /day)			
			Males age in years		Females age in years	
			1–5	19–70	1–5	19–70
DLW derived from IOM active	IOM, 2005	CTE	7.5	16.2	7.1	12.6
EPA Exposure Factors Handbook (Table 5–23)	U.S. Environmental Protection Agency, 1997	CTE	7.7	15.2	7.7	11.3
DLW derived from IOM very active	IOM, 2005	RME	8.2	18.3	8.0	14.4
Superfund default exposure factors	U.S. Environmental Protection Agency, 1991	RME	10	20	10	20

occupations, but who trained intensely as long-distance runners (Haggarty et al., 1994). Although aboriginal populations may have higher per capita energy needs, because labor-intensive resource utilization will be the mode, there is no reason to suggest that active individuals from an aboriginal population are more active than active individuals from an urban population (Haggarty et al., 1994; FAO, 2004b).

8. Discussion

The size and diversity of the DLW dataset allows estimating inhalation rates based on parameters not available from previous inhalation rate studies. Relevant parameters go beyond what is currently described (i.e., age and gender) to include PAL, BMI, pregnancy, lactation, military deployment, and marathon runners (Institute of Medicine, 2005). There is consensus that human energy expenditure occurs within a fairly narrow range of activity levels (i.e., PALs in the range of 1.4–2.4)(Westerterp, 2001). This range has been reflected in the studies described herein as well in consensus documents issued by the IOM and the FAO which analyzed energy expenditure data from a globally diverse collection of human subjects.

Estimates based on DLW are consistent with previous findings of (Layton, 1993) and the Exposure Factors Handbook (U.S. Environmental Protection Agency, 1997). Inhalation rates based on the IOM active classification are consistent with CTE (mean) inhalation rates recommended by the Exposure Factors Handbook (U.S. Environmental Protection Agency, 1997). However, inhalation rates based on the very active classification are lower than RME rates recommend by the Superfund program of the U.S. Environmental Protection Agency (U.S. Environmental Protection Agency, 1991). DLW-based estimates are suggested as an improvement to previous inhalation rates estimates to reduce uncertainty while improving accuracy, representativeness, and consistency.

Acknowledgements

David Layton for using energy expenditure to estimate inhalation rates. Damon Delistraty for his careful review.

Disclaimer

The views and opinions of author, expressed herein, do not state or reflect those of the United States Government or the Environmental Protection Agency.

References

- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MB, Coward WA. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 1993;93:572–9.
- Black AE, Coward WA, Cole TJ, Prentice AM. Human energy expenditure in affluent societies: an analysis of 574 doubly-labeled water measurements. *Eur J Clin Nutr* 1996;50:72–92.
- Brooks GA, Butte NF, Rand WM, Flatt JP, Caballero B. Chronicle of the Institute of Medicine physical activity recommendation: how a physical activity recommendation came to be among dietary recommendations. *Am J Clin Nutr* 2004;79:921S–30S.
- Esparza J, Fox C, Harper IT, Bennett PH, Schulz LO, Valencia ME, Ravussin E. Daily energy expenditure in Mexican and USA Pima indians: low physical activity as a possible cause of obesity. *Int J Obes Relat Metab Disord* 2000;24:55–9.
- Food and Agriculture Organization of the United Nations (FAO), 2004a. Human energy requirements: Report of a Joint FAO/WHO/UNU Expert Consultation pp. 107. United Nations, World Health Organization, Food and Agriculture Organization: Roma, Italy. ISBN: 9251052123; ISSN: 1813–3932 http://www.fao.org/documents/show_cdr.asp?url_file=/docrep/007/y5686e/y5686e00.htm.
- Food and Agriculture Organization of the United Nations (FAO), 2004b. Population energy requirements software (included in the Human energy requirements: Report of a Joint FAO/WHO/UNU Expert Consultation), Vol. 2005. pp. 107. United Nations, World Health Organization, Food and Agriculture Organization: Roma, Italy. http://www.fao.org/documents/show_cdr.asp?url_file=/docrep/007/y5686e/y5686e00.htm.
- Garrow JS. Treat obesity seriously. Edinburgh: Churchill Livingstone; 1988.
- Haggarty P, McNeill G, Manneh MK, Davidson L, Milne E, Duncan G, Ashton J. The influence of exercise on the energy requirements of adult males in the UK. *Br J Nutr* 1994;72:799–813.
- Harper BL, Flett B, Harris S, Abeyta C, Kirschner F. The Spokane Tribe's Multipathway subsistence exposure scenario and screening level RME. *Risk Anal* 2002;22:513–26.
- Harper BL, Flett B, Harris S, Abeyta C, Kirschner F. Response to Letter to the Editor. *Risk Anal* 2003;23:861–4.
- Institute of Medicine. Doubly Labeled Water Data Set — used to establish the estimated average requirement for energy, vol. 2005. Washington, DC: National Academies of Science, Food and Nutrition Board; 2005. p. 1357. <http://www.iom.edu/file.asp?id=7302>.
- Institute of Medicine (IOM) Panel on Macronutrients. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: National Academies Press; 2005.
- Layton DW. Metabolically consistent breathing rates for use in dose assessments. *Health Phys* 1993;64:23–36.
- Schoeller DA. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 1999;129:1765–8.
- Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. *Hum Nutr Clin Nutr* 1985;39(Suppl 1):5–41.
- Shetty P. Human energy requirements: where are we now? Issues emerging from the 2001 Expert Consultation on Energy in Human Nutrition. *Food Nutr Agric* 2002;5–11.
- Stifelman ML. Letter to the Editor Re: The Spokane Tribe's multipathway subsistence exposure scenario and screening level RME. *Risk Anal* 2003;23:859–60 author reply 861–4.

- U.S. Environmental Protection Agency. Human health evaluation manual, supplemental guidance: standard default exposure factors. Washington, DC: Office of Emergency and Remedial Response; 1991. OERR Publication 9285.6–03 NTIS PB91–921314.
- U.S. Environmental Protection Agency. Exposure Factors Handbook. Washington D.C.: U.S. Environmental Protection Agency, Office of Research and Development; 1997. EPA/600/P-95/002Fc. <http://www.epa.gov/ncea/exposfac.htm>.
- U.S. Environmental Protection Agency Office of Solid Waste And Emergency Response. Risk Assessment Guidance for Superfund Human Health Evaluation Manual Part A Interim Final. Washington, D.C.: U.S. Environmental Protection Agency; 1989. 9285.701A. <http://www.epa.gov/superfund/programs/risk/ragsa/index.htm>.
- Westerterp KR. Alterations in energy balance with exercise. *Am J Clin Nutr* 1998;68:970S–4S.
- Westerterp KR. Limits to sustainable human metabolic rate. *J Exp Biol* 2001;204:3183–7.
- Westerterp KR, Saris WH, van Es M, ten Hoor F. Use of the doubly labeled water technique in humans during heavy sustained exercise. *J Appl Physiol* 1986;61:2162–7.